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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,791	11/13/2003	Roberto Romero	4239-67284-01	8756

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EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/713,791	ROMERO ET AL.	
	Examiner	Art Unit	
	Leon Y Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-82* is/are pending in the application.

4a) Of the above claim(s) *17-32,36 and 39-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,33-35,37 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *21 September 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The use of the trademark names Ciphergen H4 and H50 has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-16, 33-35, and 37-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. In claim 1, line 3, the phrase "associated with" is vague and indefinite. The specification does not define the phrase and it is unclear how the "biomarker" (line 3) is associated with the "intra-amniotic inflammation" (lines 3-4).

4. In claim 2, the phrase "adsorbent is an antibody immobilized on a solid substrate is vague and indefinite". It is unclear whether the claimed adsorbent includes the solid substrate or if the claimed adsorbent consists only of the antibody.

5. In claim 7, line 2, the phrase "hydrophobic adsorbent" is vague and indefinite. It is unclear whether the claimed phrase refers to an adsorbent that is purely hydrophobic or an adsorbent that has hydrophobic portions. If the adsorbent is an antibody, as is claimed in claim 2, does an antibody with both hydrophilic and hydrophobic epitopes fall within the claimed invention?

6. In claims 10, 12, 14, and 37-38, the term "(alpha-defensin 1)" is vague and indefinite. It is unclear how the term limits the instant claims and how the term is related to the limitation "HNP-1".

7. In claim 33, line 1, the term "qualifying" is vague and indefinite. The specification does not define the term and it is unclear what is being claimed. How the does instant term limit the phrase "the risk of preterm delivery" (line 1)?

8. In claim 37, the term "(alpha-defensin 2)" is vague and indefinite. It is unclear how the term limits the instant claim and how the term is related to the limitation "HNP-2".

9. Claim 1 recites the limitation "said mixture" in line 4. There is insufficient antecedent basis for this limitation in the claim. Line 3 of the instant claim recites the step of "mixing an adsorbent", but there is not recitation of a "mixture".

10. Claim 8 contains the trademark/trade names Ciphergen H4 and H50. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-3, 15-16, 33, and 35 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Hitomi et al (US 5,976,832).

In the instant claims, Hitomi et al reference teaches an assay of CAAF1 (i.e. calgranulin) in amniotic fluid on an ELISA plate for the diagnosis of inflammatory disease (i.e. mixing an adsorbent that binds to at least one biomarker associated with intra-amniotic inflammation with a sample of amniotic fluid and then monitoring said mixture for binding between said biomarker and said adsorbent, wherein said assay detects at least one biomarker that is a calgranulin; analyzing a sample of amniotic fluid from said subject for a level of at least one calgranulin). See column 21, line 55 to column 22, line 58, especially column 21, lines 56-66 and column 22, lines 52-58.

With regards to claims 2-3, Hitomi et al reference teaches coating of monoclonal antibodies in an ELISA plate (i.e. antibody immobilized on a solid substrate; ELISA). See column 21, lines 59-61.

With regards to claim 15, Hitomi et al reference teaches MRP8 as a member of the S100 protein family. See column 1, lines 29-30.

With regards to claims 16 and 35, Hitomi et al reference teaches assay of CAAF1 (i.e. calgranulin C), as stated above. See column 21, line 57.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 4-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hitomi et al (US 5,976,832) in view of Krone et al (Analytical Biochemistry, 1997, vol. 244, pages 124-132).

Hitomi et al reference has been disclosed above, but fails to teach that the solid substrate is a probe (claim 4) and said biomarker is detected by laser desorption/ionization mass spectrometry (claim 5).

Krone et al reference teaches a BIAcore CM5 biosensor chip (i.e. probe) covalently derivatized with an antibody, and wherein species detected during surface plasmon resonance for biomolecular interaction analysis is interfaced with MALDI mass spectrometry (i.e. laser desorption/ionization mass spectrometry), in order to perform ligand identification and quantitation, and allow for the rapid, sensitive, and accurate investigations of biomolecular interactions. See page 125, right column, 1st full paragraph to page 126, left column, 1st full paragraph; and page 131, right column, 1st full paragraph.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Hitomi et al with a BIAcore CM5 biosensor chip (i.e. probe) covalently derivatized with an antibody, wherein species detected during surface plasmon resonance for biomolecular interaction analysis is interfaced with MALDI mass spectrometry (i.e. laser desorption/ionization mass spectrometry), as taught by Krone et al, in order to perform ligand identification and quantitation, and allow for the rapid, sensitive, and accurate investigations of biomolecular interactions. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a BIAcore CM5 biosensor chip and detection by MALDI mass spectrometry, as taught by Krone et al, in the method of Hitomi et al, since Hitomi et al teach binding interactions between antigen and antibody, and the chip and detection method of Krone

et al are used to detect antigen binding to the covalently immobilized antibody on the chip surface.

With regards to claim 5, Krone et al reference teaches MALDI mass spectrometry, as stated above. See page 125, right column, 1st full paragraph.

With regards to claim 6, Krone et al reference teaches that the chip is covalently derivatized with an antibody (i.e. adsorbent is immobilized). See page 125, right column 2nd full paragraph, lines 1-4.

With regards to claim 7, Hitomi et al reference teaches anti-CAAF1 monoclonal antibody CAAF1-22-5 (i.e. hydrophobic adsorbent). See column 21, lines 57-58.

17. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hitomi et al (US 5,976,832) in view of Krone et al (Analytical Biochemistry, 1997, vol. 244, pages 124-132) as applied to claims 1 and 6-7 above, and further in view of Pham (US 2002/0060290).

Hitomi et al and Krone et al references have been disclosed above, but fail to teach that said probe is a Ciphergen H4 probe.

Pham reference teaches a hydrophobic H4 chip from Ciphergen Biosystems, Inc. in order to provide a substrate with a reverse phase adsorbent for hydrophobic interactions. See page 5, sections 0073-0079.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Hitomi et al and Krone et al with a hydrophobic H4 chip from Ciphergen Biosystems, Inc. as taught by Pham, in order to provide a

substrate with a reverse phase adsorbent for hydrophobic interactions. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in including a Ciphergen H4 probe, as taught by Pham, in the method of Hitomi et al, Vogl et al, and Krone et al, since Hitomi et al and Krone et al teach the method of detecting analytes with immobilized antibodies on a chip surface, and the Ciphergen H4 probe is one example of a chip with the capability to immobilize adsorbents on a surface to bind analytes.

18. Claims 9-12, 34, and 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hitomi et al (US 5,976,832) in view of Heine et al (US 6,174,664 B1).

Hitomi et al reference has been disclosed and additionally teaches an ELISA assay with wells for either a standard substance or specimens. See column 21, lines 62-67. However, Hitomi et al reference fails to teach tests for the presence of at least one defensin in said sample of amniotic fluid (claims 9, 11, and 34), and that said defensin is HNP-1 (claims 10, 12, and 37-38).

Heine et al reference teaches monoclonal antibodies to defensins HNP1-3 can be prepared for an ELISA in 96-well plates, in order to screen a pregnant patient for the presence of an intraamniotic infection using amniotic fluid. See column 6, line 47 to column 7, line 52, especially column 6, lines 47-62 and column 7, lines 37-41.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Hitomi et al with monoclonal antibodies to defensins HNP1-3 can be prepared for an ELISA in 96-well plates, as taught by Heine et al, in

order to screen a pregnant patient for the presence of an intraamniotic infection using amniotic fluid. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including testing for defensins HNP1-3, as taught by Heine et al, in the method of Hitomi et al and Vogl et al, since Hitomi et al teach ELISA assays, and the testing for HNP1-3 as taught by Heine et al are also performed using ELISA assays. In addition, Hitomi et al reference teach an ELISA plate with wells for either a standard substance or specimen, thereby providing the capability of assaying for different samples, including assaying for HNP1-3 as taught by Heine et al.

19. Claims 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hitomi et al (US 5,976,832) in view of Krone et al (Analytical Biochemistry, 1997, vol. 244, pages 124-132) as applied to claims 1-2 and 4-5 above, and in further view of Heine et al (US 6,174,664 B1).

Hitomi et al and Krone et al references have been disclosed, but fail to teach tests for the presence of at least one defensin in said sample of amniotic fluid (claim 13), and that said defensin is HNP-1 (claim 14).

Heine et al reference teaches monoclonal antibodies to defensins HNP1-3 can be prepared for an ELISA in 96-well plates, in order to screen a pregnant patient for the presence of an intraamniotic infection using amniotic fluid. See column 6, line 47 to column 7, line 52, especially column 6, lines 47-62 and column 7, lines 37-41.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Hitomi et al and Krone et al, with monoclonal

antibodies to defensins HNP1-3 can be prepared for an ELISA in 96-well plates, as taught by Heine et al, in order to screen a pregnant patient for the presence of an intraamniotic infection using amniotic fluid. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including testing for defensins HNP1-3, as taught by Heine et al, in the method of Hitomi et al, Vogl et al, and Krone et al, since Hitomi et al and Krone et al teach assays to detect antigen binding using immobilized antibodies, and the testing for HNP1-3 as taught by Heine et al are also performed using antibodies. In addition, Hitomi et al reference teaches an ELISA plate with wells for either a standard substance or specimen, thereby providing the capability of assaying for different samples, including assaying for HNP1-3 as taught by Heine et al.

Conclusion

20. No claims are allowed.

21. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure:

Hutchens et al (US 5,719,060) teach desorption and ionization of analytes to analyze proteins or biomolecules.

Hitomi et al (US 6,313,267 B1) teach calcium-binding protein CAAF1 in amniotic fluid and serum.

Harrison et al (The Journal of Biological Chemistry, 1999, vol. 274, no. 13, pages 8561-8569) teach that MPR8 is calgranulin A.

Hitomi et al (Journal of Cell Science, 1996, vol. 109, pages 805-815) teach CAAF1 in ELISA studies.

Ilg et al (Biochemical and Biophysical Research Communications, 1996, vol. 225, pages 146-150) teach that CAAF1 is calgranulin C.

Panyutich et al (Journal of Immunological Methods, 1991, vol. 141, pages 149-155) teach an enzyme immunoassay for defensins.

Passey et al (Journal or Immunology, 1999, vol. 163, pages 2209-2216) teach S100A8 as a regulator of inflammation and expressed during regulation of maternal cell infiltration of the embryo.

Vogl et al (The Journal of Biological Chemistry, 1999, vol. 274, no. 36, pages 25291-25296) teach antibodies to MRP8 (i.e. calgranulin A).

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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03/17/05